

REMARKS

Applicants respectfully request that the drawings originally filed with the application be replaced with the attached substitute drawings. The second page of figure 1 was erroneously omitted from the application and the figure sheets were numbered incorrectly. The missing part of figure 1 was included in the PCT application from which the present application claims priority. The missing part of figure 1 is discussed on page 2, lines 5-14, of the application and in the claims.

The replacement of the originally filed drawings with the attached drawings does not add new matter to the application as one skilled in the art could determine the information presented in the missing part of figure 1 from the application as filed. The amino acid sequence of the light chain is given in Figure 5 and Figure 6. The corresponding nucleotide sequence can be found in Figure 3b (underlined nucleotides 2603 to 2923). The CDRs of both the heavy chain and the light chain can be obtained by applying the Kabat scheme as stated on the first part of Figure 1. In the Kabat scheme, commonly known rules for determining the CDRs are summarized. The Kabat scheme is based on a database which is freely available in the internet (see the attached paper Johnson and Wu, *Nucleic Acids Research*, 28: 214-218, 2000). A version of the Kabat scheme which is easy to apply to given sequences can be found on the home page of the University College London. When applying the rules given in the chapter "How to Identify the CDRs by Looking at the Sequence", it can be verified that the rules hold for H1, H2 and H3 in Figure 1 as filed. H1 always starts 9 residues after a cysteine (4 after cysteine according to the AbM definition

plus 5 additional amino acids), and the residue after is tryptophan. Thus, the underlined sequence of H1 is obtained. The length is 5 amino acids which is the length of the AbM definition (10 residues) minus 5 residues due to the later start. H2 starts 15 amino acids after the end of H1 and is succeeded by Arg-Phe-Thr, leading to the underlined sequence of H2 having a length of 17 residues. H3 starts 33 residues after the end of H2 and is succeeded by Trp-Gly-XXX-Gly, leading to the sequence marked in Figure 1 with a length of 10 residues. Thus a person skilled in the art would conclude that L1, L2 and L3 are to be determined by applying the Kabat scheme to the light chain.

According to the rules, L1 starts at position 24 of the sequence, and the preceding residue is always at cysteine. The length is 10 to 17 residues, and the succeeding sequence is always tryptophan, followed by tyrosine and glutamine, for instance. Thus, the sequence of L1 is unambiguously the sequence as underlined in the second part of Figure 1. L2 starts 16 residues after the end of L1 and has a length of 7 residues, leading to the sequence of L2 as given in Figure 1. Additionally, the preceding residues are isoleucine and tyrosine, which also complies with the rules. L3 always starts 33 residues after the end of L2 and the preceding residue is cysteine. The length is 7 to 11 residues, and the succeeding sequence is Phe-Gly-XXX-Gly. Thus, L3 is the sequence as underlined in Figure 1.

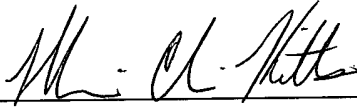
In view of the above discussion, applicants contend that the replacement of the originally filed figures with the attached figures would not add new matter to the application. However, the addition of the missing part of figure 1 would

make it significantly easier for one skilled in the art to read the present application since they would not need to repeat the above discussed calculations to determine the CDRs.

Please charge any fee deficiency or credit any overpayment to Deposit Account No. 02-2135.

Respectfully submitted,

By



Monica Chin Kitts
Attorney for Applicants
Registration No. 36,105
ROTHWELL, FIGG, ERNST & MANBECK, p.c.
Suite 800, 1425 K Street, N.W.
Washington, D.C. 20005
Telephone: (202)783-6040